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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,487	10/29/2003	Malte Buchholz	21460 US	7548
151 7590 02/06/2007 HOFFMANN-LA ROCHE INC. PATENT LAW DEPARTMENT 340 KINGSLAND STREET NUTLEY, NJ 07110			EXAMINER UNGAR, SUSAN NMN	
			ART UNIT	PAPER NUMBER
			1642	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/06/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/696,487	BUCHHOLZ ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 30 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) 4-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 4-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/23/04, 4/30/04</u> | 6) <input type="checkbox"/> Other: _____ |

1. The Election filed October 30, 2006 in response to the Office Action of September 25, 2006 is acknowledged and has been entered. Claims 1-3, drawn to limitations other than nucleic acids and claims 4-12 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-3 drawn only to methods of diagnosis of pancreatic cancer comprising detecting nucleic acid encoding UKW are currently under prosecution.
2. Applicant's election with traverse of Group 1, claims 1-3 drawn to nucleic acid diagnostic assay is acknowledged. The traversal is on the ground(s) that search of the inventions of Groups 1-3 would overlap to such an extent that the search results would be small enough to consolidate and examine together with respect to claims 1-3. The argument has been considered but has not been found persuasive because although the subject matter of Groups 1-3 might overlap, the searches are not coextensive. Different searches and issues are involved in the examination of each group and the inventions are classified in different classes and require different searches in the US Patent shoes. Thus search of all of the groups together would impose a serious burden on the examiner. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.
3. It is noted that a certified copy of a foreign priority application was received in the office on November 10, 2004. However, a review of the document reveals that it is a priority document for a coat hanger and it does not appear that the priority document is related to the instant invention. Thus, a priority date of October 29, 2003 is established for the instant invention. If applicant disagrees with any rejection set forth in this office action based on examiner's establishment of a priority date of October 29, 2003, applicant is invited to submit a priority

document relevant to the instant invention and to point to the serial number, page and line where support can be found establishing an earlier priority date.

Trademarks

4. The use of the trademarks have been noted in this application. In particular on pages 5, 16 and 17 of the specification. These trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Examiner has made an effort to identify these informalities but applicant must carefully review the specification to identify and indicate where these informal errors may be found. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the presence or absence of pancreatic cancer in a patient comprising detecting SEQ ID NO:1 in a sample from said patient and comparing the amount of SEQ ID NO:1 with a predetermined standard value indicating the decision line for tumor-induced as

compared to non-tumor induced expression, does not reasonably provide enablement for determining the presence or absence of pancreatic cancer comprising detecting an amount of nucleic acid encoding UKW. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It is assumed for examination purposes, given that the specification defines "UKW" as a nucleic acid encoding **a** (emphasis added) polypeptide of SEQ ID NO:2, that UKW is any nucleic acid encoding any polypeptide of SEQ ID NO:2, that is any nucleic acid that encodes, for example, 2 amino acids of SEQ ID NO:2 wherein the encoded polypeptide is a transmembrane protein.

The specification teaches that, the term "UKW" means a nucleic acid encoding a polypeptide of SEQ ID NO:2 wherein SEQ ID NO:2 is a transmembrane protein. (see paragraph 0036 of the published application). The specification teaches that it was surprisingly found that nucleic acids coding for polypeptide UKW are overexpressed in pancreatic tumor cells, whereas expression is considerably lower in normal pancreatic cells or in tumor cells of other origin, therefore UKW is a valuable new target for specific diagnosis of pancreatic cancer (para 0005 of the published application). The specification exemplifies the relative expression of SEQ ID NO:1 in samples derived from adenocarcinomas of the pancreas (Figure 2, para 0018 of the specification), as compared to control.

One cannot extrapolate the teaching of the specification to the scope of the claim because (1) the claims as broadly recited include not only mRNA nucleic acid but also genomic nucleic acid encoding SEQ ID NO:2, (2) the claims as broadly recited are drawn to nucleic acids encoding any polypeptide comprising

only two consecutive amino acids of SEQ ID NO:2 wherein said polypeptide is a transmembrane protein.

As drawn to the broadly recited claims, one cannot extrapolate the teaching of the specification to the scope of the claims because the claims as broadly recited include not only mRNA nucleic acids but also genomic sequences. However, Pollack et al (Nature Genetics, 1999, 23:41-46) specifically teaches that in an assay of 3195 genes it was found that most genes in cancer cells are not either amplified or overexpressed (see Figure 5, page 44) and that most highly expressed genes are not amplified, and not all amplified genes are highly expressed (p. 45, col 1). Thus, in the absence of further guidance in the specification, it cannot be determined whether the gene encoding SEQ ID NO:2 is differentially expressed in pancreatic cancer cells compared to normal pancreatic cells and one would not be able to predictably use the broadly claimed invention.

As drawn to the broadly recited claims, one cannot extrapolate the teaching of the specification to the scope of the claims because the claims are drawn to a whole universe of nucleic acids encoding undefined UKW, wherein it cannot be predicted that any UKW, other than SEQ ID NO:1 is in fact in any way associated with pancreatic cancer. In particular, the claims are drawn to a whole universe of nucleic acids which share neither structure nor function with SEQ ID NO:1 and which in fact do not encode SEQ ID NO:2. In particular the specification teaches that SEQ ID NO:2 is a transmembrane protein composed of 373 amino acids. Thus since the diagnostic nucleic acid is only required to encode, for example, a polypeptide that comprises two consecutive amino acids of SEQ ID NO:2 wherein the encoded polypeptide is a transmembrane polypeptide, the diagnostic nucleic acids include nucleic acid sequences that encode polypeptides that are 99.5%

different than SEQ ID NO:2. Further, Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, if the encoding nucleic acid encodes a polypeptide that is 99.5% different from the

polypeptide encoded by SEQ ID NO:1, it could not be predicted that the encoded transmembrane protein, nor would it be expected that the encoded transmembrane protein is in any way associated with pancreatic cancer or that it would be useful for the diagnosis of pancreatic cancer. Further, it could not be predicted nor would it be expected that a nucleic acid encoding a polypeptide with 99.5% difference from the polypeptide encoded by SEQ ID NO:1 would be in any way associated with pancreatic cancer or that it would be useful for the diagnosis of pancreatic cancer because given only the information in the specification as originally filed and the art of record, one could not predictably distinguish between those nucleic acids that would function as claimed and those that would not with a reasonable expectation of success.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the method would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

7. Claim 1 is rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claim 1 is drawn to a method of diagnosing the presence or absence of pancreatic cancer comprising detecting an amount of nucleic acid encoding UKW wherein UKW is defined in the specification as a nucleic acid encoding a (emphasis added) polypeptide of SEQ ID NO:2, that is UKW is any nucleic acid encoding a polypeptide of SEQ ID NO:2, that is any nucleic acid that encodes, for

example, 2 amino acids of SEQ ID NO:2 wherein the encode polypeptide is a transmembrane protein.

The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.*

Finally, the court addressed the manner by which a genus of cDNAs might be described. “A description of a genus of cDNAs may be achieved by means of a

recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. ” Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, per Lilly by structurally describing a representative number of UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, or by describing “structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Alternatively, per Enzo, the specification can

show that the claimed invention is complete “by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.”

In this case, the specification does not describe the UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient required to practice the claimed method in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient,, nor does the specification provide any partial structure of such UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient,, nor any physical or chemical characteristics of the UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, nor any functional characteristics coupled with a known or disclosed correlation between structure and function other than SEQ ID NO:1. Although the specification discloses a single UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, this does not provide a description of UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, that would satisfy the standard set out in Enzo.

The specification also fails to describe the UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, by the test set out in Lilly. The specification describes only a single UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, Therefore, it necessarily fails to describe a “representative number” of

such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

Thus, the specification does not provide an adequate written description of the UKW nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, that is required to practice the claimed invention. Since the specification fails to adequately describe the product to be detected, it also fails to adequately the claimed method.

8. Claims 2-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the presence or absence of pancreatic tumor cells/pancreatic tumor/pancreatic tumor in a patient comprising detecting SEQ ID with a nucleic acid probe, does not reasonably provide enablement for detecting pancreatic tumor cells/pancreatic tumor under stringent hybridization conditions, wherein the probe is **a** (emphasis added) nucleotide sequence of SEQ ID NO:1 or a fragment thereof, a nucleotide sequence which is complementary to said sequences, a nucleic acid which hybridizes under stringent conditions/hybridizes to either set of probes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to polynucleotides that (a) hybridize under “stringent conditions”/hybridize to a nucleic acid of SEQ ID NO:1 or a fragment thereof, a nucleic acid sequence which is complementary to said sequence, nucleic acid sequences which hybridize under stringent conditions to these foresaid sequences.

This encompasses all polynucleotides that hybridize under “stringent conditions”/ “hybridize”, or are complementary to said sequences.

The specification teaches that it was surprisingly found that nucleic acids coding for polypeptide UKW are overexpressed in pancreatic tumor cells/pancreatic tumor, whereas expression is considerably lower in normal pancreatic cells or in tumor cells of other origin, therefore UKW is a valuable new target for specific diagnosis of pancreatic cancer (para 0005 of the published application). The specification exemplifies the relative expression of SEQ ID NO:1 in samples derived from adenocarcinomas of the pancreas (Figure 2, para 0018 of the specification), compared to control. The specification further teaches at paragraph 0039 of the published application that "Nucleic acid probes and primers for UKW" as used herein means nucleic acid fragments useful for the detection of UKW nucleic acids by hybridization methods. Hybridization techniques and conditions are well-known to one skilled in the art. Such hybridization conditions are, for example, moderate stringent conditions including washing with a solution of 5.times.SSC, 0.5% SDS, 1.0 mmol/l EDTA, pH 8.0, followed by hybridization at 50-60.degree. C. 5.times.SSC overnight, washing at room temperature for 40 minutes with 2.times.SSC containing 0.1% SDS and afterwards washing with 0.1.times.SSC, 0.1% SDS at 50.degree. C. for 40 min with one change of fresh solution. It is also possible to use higher temperatures for hybridization (e.g. 65-70.degree. C.) as high stringent hybridization conditions.”

It is noted, however, that the stringent hybridization conditions are not limited and that in fact, as currently constituted, the claims read on the full range of hybridization conditions from low to high, thus it is assumed for examination purposes that the hybridization conditions claimed range from low to high.

It is also noted that the specification does not define the term complementary, thus it is assumed for examination purposes that the meaning of the term is the conventional meaning of the term as taught by US Patent No. 5,912,143 that is that the term complementary refers to the natural binding of polynucleotides under permissive salt and temperature conditions and specifically teaches that complementarity between two single-stranded molecules may be “partial” or it may be “complete” (col 5, lines 19-32).

One cannot extrapolate the teaching of the specification to the scope of the claims because when given the broadest reasonable interpretation, the claims are clearly intended to encompass detection of a variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the detected nucleic acids encompassed by the claims would lack significant complementarity to SEQ ID NO:1 and **would not** share either structural or functional properties with SEQ ID NO:1 or encode proteins that share either structural or functional properties with SEQ ID NO:2. Th

In particular, one cannot extrapolate the teaching of the specification to the scope of the claims because the specification does not provide teachings or working examples which would provide sufficient guidance to allow one of skill in the art to use the multitude of polynucleotide sequences encompassed by the scope of the claims. Clearly, as set forth above, it would be expected by one of ordinary skill in the art that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims **would not** share either structural or functional properties of SEQ ID NO:1 and it would not be expected that the great majority of hybridizing nucleic acids could be used to determine the presence or absence of pancreatic cancer in a patient as claimed. Given the breadth of the

claims, it is clear that one would not be able to predictably distinguish between those nucleic acids that can be used to determine the presence or absence of pancreatic cancer in a patient as claimed and those that could not. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the method would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. Claims 2-3 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 2-3 are drawn to a method of detecting pancreatic tumor cells/pancreatic tumor comprising hybridizing samples under stringent hybridization conditions with a nucleic acid probe selected from a (emphasis added) nucleic acid sequence of SEQ ID NO:1 or a fragment thereof, a nucleic acid sequence which is complementary to said sequences and nucleic acid sequences which hybridize under stringent conditions with said sequences. It is noted that the definition of stringent conditions in the specification is not limiting and that the specification does not define "complementary". Thus, it is assumed for examination purposes that the claims read on detection of pancreatic tumor cells/pancreatic tumor by hybridization under the full range of conditions including low stringency conditions with probes comprising undefined fragments of SEQ ID NO:1, partial complements thereof and probes which hybridize under undefined stringency conditions thereto. It is noted however, that the specification provides adequate written description for a method of determining whether or not a test

sample contains pancreatic tumor cells/pancreatic tumor by detecting SEQ ID NO:1 by hybridization methods.

The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.*

Finally, the court addressed the manner by which a genus of cDNAs might be described. “A description of a genus of cDNAs may be achieved by means of a

recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. ” Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, per Lilly by structurally describing a representative number of hybridized nucleic acids which are useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, or by describing “structural features common to the members of the genus, which features constitute a substantial portion of the

genus.” Alternatively, per Enzo, the specification can show that the claimed invention is complete “by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.”

In this case, the specification does not describe the hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample required to practice the claimed method in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, nor does the specification provide any partial structure of such hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, nor any physical or chemical characteristics of the hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, nor any functional characteristics coupled with a known or disclosed correlation between structure and function other than SEQ ID NO:1. Although the specification discloses a single hybridized nucleic acid which is useful for determining the presence or absence of pancreatic cancer in a patient, this does not provide a description of hybridized nucleic acids which are useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample, that would satisfy the standard set out in Enzo.

The specification also fails to describe the hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic

tumor in a sample, by the test set out in Lilly. The specification describes only a single hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a sample. Therefore, it necessarily fails to describe a “representative number” of such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

Thus, the specification does not provide an adequate written description of the hybridized nucleic acid which is useful for determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a patient, that is required to practice the claimed invention. Since the specification fails to adequately describe the product to be detected, it also fails to adequately the claimed method.

10. If Applicant were able to overcome the rejections set forth above, Claims 2-3 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the presence or absence of pancreatic tumor cells/pancreatic tumor in a patient comprising comparing the amount of nucleic acid with a predetermined standard value indicating the decision line for tumor-induced or non-tumor-induced expression of SEQ ID NO:1, does not reasonably provide enablement for detecting pancreatic tumor cells/pancreatic tumor by comparing the approximate amount of hybridization of the test sample to an approximate amount of hybridization of a second sample originating from non-pancreatic tumor cells (claim 2)/no control (claim 3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification teaches that it was surprisingly found that nucleic acids coding for polypeptide UKW are overexpressed in pancreatic tumor cells/pancreatic tumor, whereas expression is considerably lower in normal pancreatic cells or in tumor cells of other origin, therefore UKW is a valuable new target for specific diagnosis of pancreatic cancer (para 0005 of the published application). The specification exemplifies the relative expression of SEQ ID NO:1 in samples derived from adenocarcinomas of the pancreas (Figure 2, para 0018 of the specification), compared to control.

One cannot extrapolate the teaching of the specification to the scope of the claims because Stites et al (Basic and Clinical Immunology, 7th Ed, Appleton and Lange, Norwalk, 1991, page 260) specifically teaches that when any diagnostic test is used to make a decision, there is some probability of drawing an erroneous conclusion and that predictive value theory can be used to deal with this problem. The reference further teaches that diagnostic sensitivity is defined as the fraction of diseased subjects with abnormal test results and that diagnostic specificity is defined as the fraction of nondiseased subjects who have a normal laboratory test. Further, Stites et al teach that the positive predictive value is the fraction of abnormal tests that represent disease and the negative predictive value is the fraction of normal tests that represent the absence of disease (p. 260, col 1). Stites et al specifically teach that diagnostic sensitivity and specificity reveal something about the test *given prior knowledge about the disease status* (emphasis in the original document), whereas positive and negative predictive values *estimate the likelihood of disease given the test result* (emphasis in the original document). Clearly it is the latter case that is of interest when trying to make a diagnosis (p. 260, para bridging cols 1 and 2). The difficulty with the determination of the

positive predictive value for the claimed assay, is that neither the claims nor the specification provide guidance on how to determine that number. Although the specification suggests that SEQ ID NO:1 is overexpressed in pancreatic tumor cells/pancreatic tumor, whereas expression is considerably lower in normal pancreatic cells or in tumor cells of other origin, the specification makes clear that both normal pancreatic cells and cells with chronic pancreatitis express SEQ ID NO:1 and it is clear that in the absence of a control (Claim 3) and with a control of just a single individual, it could not be predicted that one could distinguish between patients that present with pancreatic cancer and those that do not. Given that claim 1 is drawn to the critical decision line, it is clear that Applicant is aware of the critical nature of this cut-off point. The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention as currently claimed would function as claimed with a reasonable expectation of success in the absence of a predictable and reliable decision line/cut-off point for determining the presence or absence of pancreatic cancer. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

11. If Applicant were able to overcome the rejection set forth above, Claim 3 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the presence or absence of assaying a sample of the patient selected from the group consisting of body fluid, cells, cell extracts or patient cells grown in culture, does not reasonably provide enablement for detecting pancreatic tumor in a sample of supernatants of cultured patient cells. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to determining the presence or absence comprising assaying a sample of the supernatant of patient cells grown in culture.

The specification teaches at paragraphs 0019 and 0020 of the specification that “According to a further aspect of the present invention, a method for the detection of pancreatic tumors, comprises incubating a sample of a patient suspected of suffering from pancreatic cancer, selected from the group of body fluid, of cells, or of a cell extract or cell culture supernatants of said cells”. Further at paragraph 0061, the specification states that “The isolation of the protein can be carried out according to known methods from the host cell or from the culture supernatant of the host cell”.

One cannot extrapolate the teaching of the specification to the scope of the claims because there is no teaching in the specification of how it would be expected that nucleic acid SEQ ID NO:1/encoding SEQ ID NO:2 would be extruded into the supernatant of the cell culture. Although it is well known that some proteins are released into the supernatant and although it is possible that some cells in the culture might be expected to burst under culture conditions and thereby release their nucleic acid, it would not be expected that the released nucleic acid would be of sufficient concentration to be detectable with current assay protocols.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention as currently claimed would function as claimed with a reasonable expectation of success in the absence of a

predictable and reliable decision line/cut-off point for determining the presence or absence of pancreatic cancer. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

12. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 are indefinite because none of claims 1-3 contain a positive process step which clearly relates back to the preamble.

Claim 1 is indefinite in the recitation of the phrase “an amount of nucleic acid”. The claim is indefinite because it is unclear what “amount” is being claimed. For example, is the entire amount in the sample being detected? Is only a partial amount being detected? The limitation of “an amount” is a relative limitation which renders the claim indefinite. The limitation is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 2 is indefinite in the recitation of “stringent hybridization conditions”. stringent conditions are not defined by the claim (which reads on the full range of stringent conditions, that is from very permissive to very high stringency), the specification does not provide a standard for ascertaining the requisite degree of stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

Claim 2 is indefinite in the recitation of the phrase “greater amount”. The phrase is a relative phrase, is not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 2 is indefinite in the recitation of determining whether or not a test sample of tissue or fluid of a patient is “derived from pancreatic tumor cells”. The claims are confusing because the meaning of the term “derived” as drawn to the tumor cells is unknown. Does Applicant intend, for example, the claim to mean that the sample is made up of tumor cell cytoplasm? Does Applicant intend, for example that the sample is a tissue sample that is somehow derived from tumor cells? The metes and bounds of the claim cannot be determined from the claim or the specification as originally filed. Clarification is required.

Claim 3 is indefinite in the recitation of the term “preferably”. The term “preferably renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 3 is indefinite in the recitation of the phrase “or a mixture of nucleic acids”. The claim is indefinite because there is no antecedent basis for the phrase in the claim as currently constituted and it cannot be determined from the claim language what the mixture of nucleic acids might refer to.

Claim 3 is indefinite because it is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are a control for comparison in order to determine the presence or absence of pancreatic cancer.

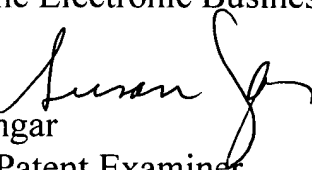
13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is

(571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898.. The fax phone number for this Art Unit is (571) 273-8300.

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Susan Ungar
Primary Patent Examiner
January 3, 2007